

**Remarks****Summary of Status of Amendments and Office Action**

In the present amendment, claim 1 is amended. Claims 2 and 11-20 have been previously canceled. In this amendment, claims 3 and 5 are canceled. All claims have been canceled without prejudice or disclaimer to the subject matter recited therein. Therefore, claims 1, 4, and 6-10 are pending in the application with claim 1 being independent.

Claim 1 is amended to recite claim language recited in claims 3 and 5, which are canceled by the above amendment. Claim 1 is also amended to recite "choosing at least one template protein among the reference proteins that has highest similarity in three-dimensional structure to the protein comprising the query sequence based on the matching score of the whole sequence...". Support for this amendment is found in the specification, for example, at page 10, line 17. Examples of calculation of the matching score are given at page 20, line 2,1 to page 21, line 11. Claim 6 is amended to revise the claim dependency. No new matter is added.

**Amendment filed under 37 CFR 1.114**

Applicant expresses appreciation for entrance of the Amendment filed under 37 CFR 1.114 on April 14, 2005, and for withdrawing the finality of the previous Office Action.

**Response to § 112, Second Paragraph Rejections**

Claims 1 and 3-10 are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite because there is allegedly a disconnect between the method regarding the “conducting” operation and the “choosing” operation. The rejection asserts that the “conducting” operation involves “matching based on the environmental information on each amino acid residue,” and that the “choosing” operation involves choosing a “template protein among the reference proteins that has highest similarity in three-dimensional structure to the protein.” The rejection then asserts that the “choosing” operation is based solely on the similarity of the three-dimensional structure of the reference proteins and the query protein, and that there is allegedly a disconnect between how the reference proteins identified in the “conducting” operation are related to the “choosing” operation.

Applicant submits that the relationship between the reference proteins of the “conducting” process and their use for obtaining a “matching score” recited in the “choosing” process is in fact clear and definite. One of ordinary skill in the art would look to the specification for the meaning of “environmental information” recited in the “conducting” process. It is defined at page 11, lines 5-8, as meaning “mainly the degree of exposure to the protein surface and the environment of the side chain group of each amino acid residue in the three-dimensional structure of the reference protein.” Also, “environmental information” is further described in relation to “three-dimensional structures” at page 12, lines 23-30: “The methods of the present invention consider these variety of three-dimensional structures of proteins, it enables to give scores reflecting the environment of each amino acid residue.” Further, the “choosing” process of claim 1 recites “choosing at

least one template protein among the reference proteins that has highest similarity in three-dimensional structure to the protein comprising the query sequence based on the matching score of the whole sequence...”. Accordingly, one of skill in the art reading the specification would understand that the environmental information comprises, at least in part, scores based on the three-dimensional structures of the proteins. Thus, one of skill in the art reading the claims and the specification would understand the clear and definite relationship between the recited reference proteins of the “conducting” process and the recited reference proteins of the “choosing” process.

In view of the foregoing, Applicant respectfully requests withdrawal of the rejections under 35 U.S.C. § 112, second paragraph.

#### **Response to 35 U.S.C. § 102(b) Rejection**

Claims 1 and 3-10 are rejected under 35 U.S.C. § 102(b) as being anticipated by U.S. Patent No. 6,436,850 to Eisenberg et al. (“Eisenberg”). The rejection asserts that Eisenberg discloses that all sequences in its database of target sequences are aligned with 3D structure profile using a dynamic programming, which allows insertions and deletions (or gaps) in the alignment.

The rejection admits that Eisenberg does not explicitly disclose that the comparison of the sequences involves the segmentation of the reference protein into two or more segments. The rejection, however, alleges that the use of two or more segments is inherently disclosed by Eisenberg’s use of the dynamic programming algorithm. In particular, the rejection alleges that Eisenberg’s dynamic programming algorithm involves

segmentation of the N and C termini segments so that the claimed invention is anticipated. To support this assertion, the rejection cites U.S. Patent No. 6,512,981 also to Eisenberg et al. ("Eisenberg-2"). The rejection appears to point to the disclosure in Eisenberg-2 at column 9, lines 47-51, as alleged evidence showing that Eisenberg's dynamic programming algorithm involves segmentation of the N and C termini segments. Applicant traverses the rejection for reasons of record, and for the following reasons.

Applicant points out that claim 1 now recites the claim language of claims 3 and 5, now canceled. These amendments even more clearly describe the processes of dividing a core segment sequence and the nature of the core segment sequence as discussed above in the response to the indefiniteness rejection. Further, even though Eisenberg implicitly suggests a division of a full sequence by using a gap and the use of two or more resulting segments, Eisenberg fails to teach an intentional division of a sequence to obtain a core segment sequence recited in the claims. For example, Eisenberg does not teach or suggest a method wherein the amino acid sequence of each of the reference proteins is divided into one or more core segment sequences which are predetermined to form a hydrophobic core, and into one or more sub segment sequences which are not predetermined to form a hydrophobic core. Furthermore, Eisenberg also fails to teach or suggest performing a matching process by sliding the two or more core segment sequences of the reference protein on the query sequence without consideration of any gaps except those at one end or both ends of the core segment sequence, wherein the reference proteins are divided into one or more core segment sequences as discussed above.

The rejection asserts that the claim term “core segment” is not specifically defined, and that there is no support for the term. Accordingly, the rejection broadly interprets that the recited term “core sequence” is thus not distinguishable from “any segment comprising two or more contiguous amino acid residues”, and therefore the claims are anticipated by Eisenberg. Applicant points to the use of the term “core segment” in the specification, as follows: “It is possible to regard certain segment sequences as core segment sequences which form secondary structures such as  $\alpha$ -helix structure and  $\beta$ -strand structure and substantially participate in the formation of a hydrophobic core, and other segments as sub segment sequences.” Page 16, lines 10-21, emphasis added. Applicant submits that Eisenberg does not teach or suggest “two or more core segment sequences of the reference protein” as recited in the claims.

Further, Applicant submits that there is no teaching or suggestion in Eisenberg that “each of the reference proteins is divided into one or more core segment sequences which are predetermined to form a hydrophobic core, and into one or more sub segment sequences which are not predetermined to form a hydrophobic core”, as recited in the instant claims.

Thus, for the above reasons, the claims are not anticipated by Eisenberg or by Eisenberg combined with the inherent teachings of Eisenberg-2. Therefore, Applicant respectfully requests reconsideration and withdrawal of the rejection of claims under 35 U.S.C. §102(b).

**Response to 35 U.S.C. § 102(e) Rejection**

Claims 1 and 3-10 are rejected under 35 U.S.C. § 102(e) as being anticipated by U.S. Patent No. 5,878,373 to Cohen et al. ("Cohen"). The rejection alleges that Cohen discloses all limitations of the claims. In particular, the rejection asserts Cohen's "cluster vector" (col. 4, lines 1-11) discloses the recited amino acid sequence of each of the reference proteins divided into two or more segment sequences comprising two or more contiguous amino acid residues. The rejection also alleges that the claimed matching based on the environmental information on each amino acid residue of each of the two or more core segment sequences of the reference protein and hydrophobicity or hydrophilicity property of the side chain of each amino acid residue of the query sequence is disclosed at col. 3, lines 36-49 and 37-67, and col. 4, lines 7-11. Applicant traverses the rejection.

It appears that the rejection is asserting that the "cluster vector" of Cohen might be an example of a division of a reference protein sequence. However, Applicant points out that Cohen's "cluster vector" is not the same as the "core segment sequence" recited in the claims. For example, the method for generating the "cluster vector" is explained in "Third Preferred Embodiment" in col. 14 to col. 15, and specifically, the "cluster vector" is generated by extracting a short length vector so as to give a higher degree of over wrapping alignment in the three dimensional structure of the aligned set of homologous protein sequences. See, in particular, col. 15, lines 21-26. This is distinguished from the claimed invention because the claimed "core segment sequence" is prepared by choosing a partial sequence that corresponds to a

hydrophobic core of the three dimensional structure of a protein.

Accordingly, Applicant submits that there is no teaching or suggestion in Cohen for preparing reference proteins divided into one or more core segment sequences which are predetermined to form a hydrophobic core, and into one or more sub segment sequences which are not predetermined to form a hydrophobic core, as recited in the instant claims.

Thus, for the above reasons, the claims are not anticipated by Cohen. Therefore, Applicant respectfully requests reconsideration and withdrawal of the rejection of claims under 35 U.S.C. §102(e).

### CONCLUSION

In view of the forgoing, Applicant respectfully submits that all pending claims patentably define Applicant's invention. Allowance of the application with an early mailing date of the Notices of Allowance and Allowability is therefore respectfully requested.

Any comments or questions concerning this application can be directed to the undersigned at the telephone number given below.

Respectfully submitted,  
Akiko ITAI



Bruce H. Bernstein  
Reg. No. 29,027

December 12, 2005  
GREENBLUM & BERNSTEIN, P.L.C.  
1950 Roland Clarke Place  
Reston, VA 20191  
(703) 716-1191

Stephen M. Roylance  
Reg. No. 31,296